Remarks

Reconsideration and withdrawal of the rejections set forth in the Office action dated September 14, 2006 are respectfully requested.

Claims 1-18 and 21 are pending. Claims 13-18 and 21 are withdrawn. Claims 19-20 are canceled.

I. Amendments

Claim 13 is amended to improve readability.

No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. §102

Claims 1, 2, 9, 11, and 12 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Boxer *et al.* (PCT Publication No. 98/23948).

Applicants respectfully traverse these rejections.

A. The Present Claims

The present claims relate to an array of separated lipid bilayers. The array comprises (i) a substrate having a surface defining a plurality of distinct bilayer-compatible surface regions, (ii) a plurality of discrete lipid bilayer expanses in associated surface regions, the expanses having inner and outer bilayer surfaces, (iii) an aqueous film interposed between each bilayer-compatible surface region and the lower surface of the corresponding lipid bilayer expanse, (iv) a bulk aqueous phase covering the lipid bilayer expanses, and (v) at least one biomolecule anchored to at least one of the lipid bilayer expanses through a complementary oligonucleotide sequence capable of specifically hybridizing with the patch-specific oligonucleotide sequence in that expanse, such that the biomolecule is anchored to that expanse. Each of the expanses contains one or more lipids derivatized with an oligonucleotide having a patch-specific oligonucleotide sequence and extending from the outer surface of the associated expanse.

B. The Cited References

BOXER ET AL. relate to a surface detector array formed of a substrate having a surface defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions. The bilayer-compatible surface regions may further include a selected biomolecule covalently or non-covalently attached to a lipid molecule. Examples of biomolecules include polynucleotides.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

The present claims require that each of the expanses contain one or more lipids derivatized with an oligonucleotide having a patch-specific oligonucleotide sequence and extending from the outer surface of the expanse and at least one biomolecule anchored to the lipid bilayer expanse through a complementary oligonucleotide sequence. Thus, the biomolecule is anchored to the bilayer expanse through complementary binding of the oligonucleotides. Nowhere do Boxer *et al.* teach using complementary oligonucleotides to attach the biomolecule to the bilayer expanse. In contrast, Boxer *et al.* teach a biomolecule, which may be a polynucleotide, covalently or non-covalently attached to a lipid of the lipid bilayer expanse (page 5, lines 1-5). Therefore, Boxer *et al.* do not disclose each and every element of Applicants' claims. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102.

III Rejections under 35 U.S.C. §103

Claims 1, 2, and 9-12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* in view of Cornell *et al.* (U.S. Patent No. 5,874,316), Arnold *et al.* (U.S. Patent No. 5,310,648), or Bayerl *et al.* (U.S. Patent No. 6,051,372).

Claims 1-7 and 9-12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* in view of both Boukobza *et al.* (*J Phys Chem*, 105:12165-12170, 2001) and Niemeyer (DE 19902391, abstract).

Claims 1, 2, 8, 9, 11, and 12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* in view of Shen *et al.* (U.S. Publication No. 2003/0148335).

These rejections are respectfully traversed.

A. The Present Claims are described above.

B. The Cited References

BOXER ET AL. is described above.

CORNELL ET AL. relate to receptor binding of an analyte.

ARNOLD ET AL. describe an imprinted matrix which exhibits selective binding interactions through metal chelates.

BAYERL ET AL. describe two-dimensional patterning of a three-dimensional surface by a template molecule.

BOUKOBZA ET AL. describe an immobilization technique using biotin-avidin interaction. Large unilamellar lipid vesicles are attached to a glass-supported lipid bilayer through the biotin-avidin binding interaction.

NIEMEYER ET AL. states reversible, parallel, site-specific immobilization of macromolecules on a solid phase comprising using nucleic acids as immobilization-mediating reagents is new.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

1. Rejection over Boxer *et al.* in view of Cornell *et al.*, Arnold *et al.*, or Bayerl *et al.*

The deficiencies of Boxer *et al.* are discussed above. One of skill in the art would not modify the teaching of Boxer *et al.* to replace the polynucleotide biomolecule covalently or non-covalently bound to a lipid molecule of a bilayer expanse with a biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotides.

Nor do any of Cornell *et al.*, Arnold *et al.*, or Bayerl *et al.* provide the missing teaching as these references makes no mention of complementary oligonucleotides for binding of a biomolecule to the lipid bilayer expanses. Instead, each of Cornell *et al.*, Arnold *et al.*, and Bayerl *et al.* are cited for a teaching of the use of self-limiting lateral diffusion as in present claim 10.

Importantly, the present array provides a bilayer expanse that is physiologically fluid. Self-limiting lateral diffusion in the present claims is as a non-physical barrier for corralling planar lipid bilayers into discrete locations in the array. Physical barriers include modifications to the chip surface and include scratching, positive photo-resist, and gold. By contrast, self-limiting lateral diffusion results from the fact that a planar lipid bilayer deposited on a substrate will "swell" or diffuse to make its dimensions about 106% of the original dimensions, after which there is no longer further expansion or diffusion of the lipids at the borders. However, there is still diffusion and fluidity of the bilayer away from the edges of the

membrane. By contrast, each of the cited references describes methods for restricting lateral diffusion. However, these methods affect the entire membrane thereby substantially reducing the fluidity, and hence functionality, of the whole lipid bilayer expanse. This makes the lipid bilayer expanse unsuitable as a lipid bilayer array. Cornell *et al.* teach limiting diffusion by selecting lipids which are crystalline at room temperature. Arnold *et al.* teach polymerization of molecules in the membrane, and Bayerl *et al.* teach reducing the ambient temperature below the gel-fluid phase transition temperature.

2. Rejection over Boxer *et al.* in view of Boukobza *et al.* and Niemeyer

The deficiencies of Boxer *et al.* are detailed above. Nor would one of skill in the art modify Boxer *et al.* to replace the polynucleotide biomolecule covalently or non-covalently bound to a lipid molecule of a bilayer expanse with a biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotides based on the teaching of either or both of Boukobza *et al.* and Niemeyer.

Boukobza *et al.* teach using biotin-avidin affinity for binding biomolecules to surface-tethered lipid vesicles. Importantly, due to the nature of biotin-avidin affinity, the entire bilayer expanse is affected similarly. In contrast, the present array can have selective binding based on different oligonucleotide sequences.

The abstract of Niemeyer makes no mention of at least one biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotide sequences. Niemeyer teaches site-specific immobilization of biomolecules on a solid phase.

3. Rejection over Boxer *et al.* in view of Shen *et al.*

The deficiencies of Boxer *et al.* are discussed above. Nor would one of skill in the art modify Boxer *et al.* to replace the polynucleotide biomolecule covalently or non-covalently bound to a lipid molecule of a bilayer expanse with a biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotides based on the teaching in Shen *et al.* as this reference makes no mention of

complementary oligonucleotides for binding of a biomolecule to the lipid bilayer expanses. Instead, Shen *et al.* is cited for a teaching of the use of oligonucleotide identification tags to identify a non-nucleic acid target. Shen *et al.* is directed toward detecting non-nucleic acid targets, most often protein targets, in a sample. By contrast, the present claims are not concerned with assaying for the presence of non-nucleic acid targets. Instead, the oligonucleotides of the present claims are used for tethering the biomolecule to the bilayer expanse.

As the references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted

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